

Remarks

Entry of the foregoing and reconsideration of the application identified in caption as amended, pursuant to and consistent with the Rules of Practice in Patent Cases, and in light of the remarks which follow, is respectfully requested.

By the present amendment, claims 1, 2, 11, 15-18, and 20-21 have been amended so that claims 1-11, 15-18, and 20-21 will remain pending.

The specification has been amended in Table 1 to correct a typographical error with respect to C-example 2. Specifically, "1.3 fold over B" has been corrected to "1.3 fold over D." This example represents a 1.3 fold increase over example D, not B. Support for this amendment lies in a mathematical comparison of the solubility data for compositions of Examples C and D.

The specification stands objected to based upon the following informality. The specification contains the composition C-PROPOFLAVIS which appears to be a trademark/trade name of an apparent propolis-containing material. This objection is respectfully traversed.

With regard to the objection for the use of trademark Propoflavis and C-Propoflavis, applicants confirm that Propoflavis is a highly-purified propolis extract and C-Propoflavis is the propolis-containing composition according to Example 1 of the present application (see Examples 5-12). The specification has been amended accordingly, where necessary. Withdrawal of the record objection to the specification is respectfully requested.

Claim 2 stands rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for containing reference to more than one amino acid. This rejection is respectfully traversed.

Claim 2 has been amended to replace "amino acids" with "an amino acid." Withdrawal of the record rejection of claim 2 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

Claims 1-11, 15-18, 20 and 21 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims are considered indefinite because the term "quaternary" is considered internally inconsistent with a composition comprising the recited chemical compounds. This rejection is respectfully traversed.

Claims 1 and 11 have been amended to replace “comprising” with “consisting essentially of” to more particularly point out that the claimed quaternary composition is directed to the four recited components and any impurities so long as they do not materially alter the formulation.

Withdrawal of the record rejection of claims 1-11, 15-18, 20 and 21 under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 15-18 and 20-21 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention with respect to combining the ground powdered composition/formulations with excipients and non-powdered species. This rejection is respectfully traversed.

Independent claims 15-17 have been amended to recite a mixture comprising the powdered composition of claim 1 and suitable excipients or diluents to more particularly point out that the claims are directed to the use of the quaternary compositions according to the invention for preparing products, not necessarily in form of powder, by combining the quaternary compositions with the addition of acceptable excipients and diluents, for example, as disclosed in Examples 5-12.

Withdrawal of the record rejection of claims 15-18, and 20-21 under 35 U.S.C. § 112, second paragraph, is respectfully requested.

Claims 1-11, 15-18, and 20-21, stand rejected under 35 USC § 103 (a), as being obvious over Aga (A: PTO- 892, 2/1/2007) in view of Mandai (US 6,005,100) and Zaffaroni (US 3,876,816) and Kasori (JP 60188036 A-abstract). This rejection is respectfully traversed.

Claim 1 is directed to a powdery quaternary composition wherein the active substance propolis and a hydrophilic carrier are co-ground with two auxiliary co-grinding substances, one being an amino acid and the second one being glycyrrhizate.

The Examiner relies upon the apparent equivalence between the two different sweeteners glycyrrhizate and threalose as motivation for the rejection on the ground of obviousness with reference to the Aga teaching in view of Mandai, Zaffaroni and Kasori. Although this assumption could be done in some specific circumstances in the case of the use of glycyrrhizate as a sweetening agent, this assumption is groundless for the instant-application.

The claimed composition is co-ground powdered and quaternary being formed by propolis, a hydrophilic carrier, an amino acid and glycyrrhizate, wherein:

- i) the amino acid and glycyrrhizate are two auxiliary co-grinding substances;
- ii) the component glycyrrhizate is used as the second co-grinding auxiliary substance and not for its sweetening properties; and
- iii) the addition of this second co-grinding auxiliary confers the peculiar properties of solubility to the composition of the claimed invention.

These aspects are readily apparent from the disclosure and widely supported in the specification and claims. In Table 1 unexpected results obtained with the quaternary composition of the invention as compared to the ternary composition without glycyrrhizate are shown.

Furthermore, even though both trehalose and glycyrrhizate are sweeteners, they are not obvious variants as auxiliary co-grinding substances. The first, trehalose is a simple disaccharide and the latter, glycyrrhizate is a triterpenoid glycosidic saponin, respectively. An artisan skilled in the art would not be motivated from the prior art cited, where the glycyrrhizate is used as flavour-imparting/sweetening agent, to substitute glycyrrhizate with trehalose for the purpose of the present invention, i.e., for use as auxiliary co-grinding substances to increase solubility.

In fact, it is accepted law, that when the invention is more than the predictable use of prior art elements according to their established function, the invention is not obvious. As recently reiterated by the Supreme Court (*KSR International Co vs Teleflex*), the fact that the known elements work together in an unexpected and useful manner as noted above support the conclusion of non-obviousness.

The conclusion of obviousness by the Examiner is based upon viewing the claimed invention as merely a predictable combination of components to impart flavour/sweetness to the composition. This analysis overlooks the unexpected aspects of the claimed invention derived from the addition of glycyrrhizate as auxiliary co-grinding substance. Namely the increased solubility properties of the co-ground powdered quaternary compositions, comprising glycyrrhizate, in comparison to the corresponding ternary composition without glycyrrhizate.

None of the prior art references cited by the Examiner teaches or suggests that glycyrrhizate can be an auxiliary co-grinding substance, nor do they teach or suggest an

expected synergistic effect between the same and an amino acid with respect to increased solubility. Therefore, one of ordinary skill in the art would not have had a reasonable expectation of success in producing the claimed invention.

None of the prior art references cited refers to the water-solubility properties of glycyrrhizate or trehalose and from their combination it is only readily apparent that glycyrrhizate and trehalose are obvious variants for their sweetening/flavour-imparting properties, but not as co-grinding auxiliary substances nor for their water-solubility improving properties because this use and these properties were never mentioned.

In fact, Aga teaches in first instance that the water-solubility properties of a propolis extract can be improved by adjusting the pH of propolis to 5.5-7 with an organic acid (see column 3, lines 3-10 and claims). Incidentally Aga discloses compositions where the water-soluble propolis extract is dehydrated and pulverized by mixing with anhydrous saccharides (including trehalose) and/or cyclodextrins and where the water-solubility properties can be further improved by adding pH-controlling agents such as sodium bicarbonate and magnesium carbonate (see column 4, lines 15-28). Further, trehalose, together with others, is again mentioned as an agent to improve the activity, effect, stability and handleability of the propolis extract according to the invention (see column 4, lines 29-41). Hence, the teaching of Aga is to improve the water solubility of propolis acting on the pH of the propolis extract itself (see Examples A 1-4) and not by combining and pulverizing with others substances, since these substances are used for other purposes (essentially stability, flavour and taste of the propolis extract).

Mandai discloses a dessicant containing a non-reducing anhydrous trehalose suitable in combination with other chemical substances to improve the shelf life of vegetable extracts, food stuffs, cosmetics and pharmaceutical products. The anhydrous trehalose when converted in hydrous crystalline trehalose acts as stabilizer, preservative, filler and carrier (see column 10, lines 8-10) and as agent for improving the processability, flavor and meltability in the mouth (see column 10, lines 14-17). The use of anhydrous trehalose as sweetener is further mentioned (see column 15, lines 48-51 and 62-65).

Zaffaroni discloses novel nonabsorbable, non-nutritive water-soluble sweetener composition including glycyrrhizin.

Kasori discloses the addition of glycyrrhetic acid to a combination of organic salts and cyclodextrin “ to remove the defects of them in taste such as bitterness and give economically sweetening of good quality”, thus again for sweetening purposes.

Therefore, when combined together the cited prior art teaches that glycyrrhizate and trehalose are obvious variants as flavour imparting/sweetener agents. The prior art is silent on the capability of these substances to act as co-grinding agents and/or on their capability to improve the water solubility of any kind of compound, especially propolis.

The Examiner's reasoning does not properly consider that the quaternary compositions of the present invention are a complex system aimed to increase the water-solubility of a particularly insoluble active principle, such as propolis, by co-grinding the same with a hydrophilic carrier, an amino acid as first co-grinding substance and the second co-grinding auxiliary glycyrrhizate. As known to one of ordinary skill in the art, the replacement of a component with another in such a complex system does not necessarily give the same effect (i.e., water-solubility), in spite of comparable (if any) water-solubility of the components used for the purpose.

An important feature is the grinding process of propolis with a hydrophilic carrier, an amino acid as first co-grinding substance and the second co-grinding auxiliary glycyrrhizate and this aspect is clearly evidenced in the claim 1 by the word "co-ground".

Applicant has replicated the Examples 1 and 2 of the quaternary compositions disclosed in the application with the replacement of the glycyrrhizate with trehalose. The results indicate that the latter is not equivalent to glycyrrhizate, as a second auxiliary co-grinding substance, in increasing the water-solubility of the ternary co-ground compositions formed by propolis, a hydrophilic carrier and an amino acid as first auxiliary co-grinding substance.

The technical report on the tests performed by the Applicant is herein enclosed together with the Declaration Under 37 CFR §1.132.

For at least the reasons noted above, withdrawal of the record rejection of claims 1-11, 15-18, and 20-21, under 35 USC § 103 (a), as being obvious over Aga in view of Mandai, Zaffaroni, and Kasori and allowance of said claims is respectfully requested.

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such action is hereby earnestly solicited.

Respectfully submitted,

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